Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Asthma: diagnosis, monitoring and chronic asthma management.

Bibliographic Source(s)

National Guideline Centre. Asthma: diagnosis, monitoring and chronic asthma management. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov 29. 38 p. (NICE guideline; no. 80).

Guideline Status

This is the current release of the guideline.

This meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

 = Poor  = Fair  = Good  = Very Good  = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests
	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement

	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
	Search Strategy
	Study Selection
	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
	Grading the Quality or Strength of Evidence
	Benefits and Harms of Recommendations
	Evidence Summary Supporting Recommendations
	Rating the Strength of Recommendations
	Specific and Unambiguous Articulation of Recommendations
	External Review
	Updating

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Guideline Centre on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Initial Clinical Assessment

See also algorithm A in the original guideline document for initial clinical assessment in adults, young people and children with suspected asthma.

Clinical History

Take a structured clinical history in people with suspected asthma. Specifically, check for:

- Wheeze, cough or breathlessness, and any daily or seasonal variation in these symptoms
- Any triggers that make symptoms worse
- A personal or family history of atopic disorders

Do not use symptoms alone without an objective test to diagnose asthma.

Do not use a history of atopic disorders alone to diagnose asthma.

Physical Examination

Examine people with suspected asthma to identify expiratory polyphonic wheeze and signs of other causes of respiratory symptoms, but be aware that even if examination results are normal the person may still have asthma.

Initial Treatment and Objective Tests for Acute Symptoms at Presentation

Treat people immediately if they are acutely unwell at presentation, and perform objective tests for asthma (for example, fractional exhaled nitric oxide [FeNO], spirometry and peak flow variability) if the equipment is available and testing will not compromise treatment of the acute episode.

If objective tests for asthma cannot be done immediately for people who are acutely unwell at presentation, carry them out when acute symptoms have been controlled, and advise people to contact their healthcare professional immediately if they become unwell while waiting to have objective tests.

Be aware that the results of spirometry and FeNO tests may be affected in people who have been treated empirically with inhaled corticosteroids.

Testing for Asthma

Do not offer the following as diagnostic tests for asthma:

- Skin prick tests to aeroallergens
- Serum total and specific immunoglobulin E (IgE)
- Peripheral blood eosinophil count
- Exercise challenge (to adults aged 17 and over)

Use skin prick tests to aeroallergens or specific IgE tests to identify triggers after a formal diagnosis of asthma has been made.

Occupational Asthma

Check for possible occupational asthma by asking employed people with suspected new-onset asthma, or established asthma that is poorly controlled:

- Are symptoms better on days away from work?
- Are symptoms better when on holiday[1]?

Make sure all answers are recorded for later review.

Refer people with suspected occupational asthma to an occupational asthma specialist.

Diagnosing Asthma in Young Children

For children under 5 with suspected asthma, treat symptoms based on observation and clinical judgement, and review the child on a regular basis (see "Pharmacological Treatment Pathway for Children Under 5" below). If they still have symptoms when they reach 5 years, carry out objective tests (see "Objective Tests for Diagnosing Asthma in Adults, Young People and Children Aged 5 and Over" below and algorithm B in the original guideline document).

If a child is unable to perform objective tests when they are aged 5:

- Continue to treat based on observation and clinical judgement
- Try doing the tests again every 6 to 12 months until satisfactory results are obtained
- Consider referral for specialist assessment if the child repeatedly cannot perform objective tests and is not responding to treatment

Objective Tests for Diagnosing Asthma in Adults, Young People and Children Aged 5 and Over

See also Table 1 in the original guideline document for a summary of objective test threshold levels.

Diagnostic Hubs

Those responsible for planning diagnostic service support to primary care (for example, clinical commissioning groups) should consider establishing asthma diagnostic hubs to achieve economies of scale and improve the practicality of implementing the recommendations in this guideline.

Airway Inflammation Measures

Fractional Exhaled Nitric Oxide

Offer a FeNO test to adults (aged 17 and over) if a diagnosis of asthma is being considered. Regard a FeNO level of 40 parts per billion (ppb) or more as a positive test.

Consider a FeNO test in children and young people (aged 5 to 16)[2] if there is diagnostic uncertainty after initial assessment and they have either:

- Normal spirometry, or
- Obstructive spirometry with a negative bronchodilator reversibility (BDR) test.

Regard a FeNO level of 35 ppb or more as a positive test.

Be aware that a person's current smoking status can lower FeNO levels both acutely and cumulatively. However, a high level remains useful in supporting a diagnosis of asthma.

Lung Function Tests

Spirometry

Offer spirometry to adults, young people and children aged 5 and over if a diagnosis of asthma is being considered. Regard a forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) ratio of less than 70% (or below the lower limit of normal if this value is available) as a positive test for obstructive airway disease (obstructive spirometry).

Bronchodilator Reversibility

Offer a BDR test to adults (aged 17 and over) with obstructive spirometry (FEV1/FVC ratio less than 70%). Regard an improvement in FEV1 of 12% or more, together with an increase in volume of 200 ml or more, as a positive test.

Consider a BDR test in children and young people (aged 5 to 16) with obstructive spirometry (FEV1/FVC ratio less than 70%). Regard an improvement in FEV1 of 12% or more as a positive test.

Peak Expiratory Flow Variability

Monitor peak flow variability for 2 to 4 weeks in adults (aged 17 and over) if there is diagnostic uncertainty after initial assessment and a FeNO test and they have either:

- Normal spirometry, or
- Obstructive spirometry, reversible airways obstruction (positive BDR) but a FeNO level of 39 ppb or less.

Regard a value of more than 20% variability as a positive test.

Consider monitoring peak flow variability for 2 to 4 weeks in adults (aged 17 and over) if there is diagnostic uncertainty after initial assessment and they have:

- Obstructive spirometry, and
- Irreversible airways obstruction (negative BDR), and
- A FeNO level between 25 and 39 ppb.

Regard a value of more than 20% variability as a positive test.

Monitor peak flow variability for 2 to 4 weeks in children and young people (aged 5 to 16) if there is diagnostic uncertainty after initial assessment and a FeNO test and they have either:

- Normal spirometry, or
- Obstructive spirometry, irreversible airways obstruction (negative BDR) and a FeNO level of 35 ppb or more.

Regard a value of more than 20% variability as a positive test.

Airway Hyperreactivity Measures

Direct Bronchial Challenge Test with Histamine or Methacholine

Offer a direct bronchial challenge test with histamine or methacholine[3] to adults (aged 17 and over) if there is diagnostic uncertainty after a normal spirometry and either a:

- FeNO level of 40 ppb or more and no variability in peak flow readings, or
- FeNO level of 39 ppb or less with variability in peak flow readings.

Regard a PC20 value of 8 mg/ml or less as a positive test.

Consider a direct bronchial challenge test with histamine or methacholine[3] in adults (aged 17 and over) with:

- Obstructive spirometry without bronchodilator reversibility, and
- A FeNO level between 25 and 39 ppb, and
- No variability in peak flow readings (less than 20% variability over 2 to 4 weeks).

Regard a PC20 value of 8 mg/ml or less as a positive test.

If a direct bronchial challenge test with histamine or methacholine is unavailable, suspect asthma and review the diagnosis after treatment, or refer to a centre with access to a histamine or methacholine challenge test.

Diagnosis in Children and Young People Aged 5 to 16

See also algorithm B in the original guideline document for objective tests in young people and children aged 5 to 16.

Diagnose asthma in children and young people (aged 5 to 16) if they have symptoms suggestive of asthma and:

- A FeNO level of 35 ppb or more and positive peak flow variability, or
- Obstructive spirometry and positive bronchodilator reversibility.

Suspect asthma in children and young people (aged 5 to 16) if they have symptoms suggestive of asthma and:

- A FeNO level of 35 ppb or more with normal spirometry and negative peak flow variability, or
- A FeNO level of 35 ppb or more with obstructive spirometry but negative bronchodilator reversibility and no variability in peak flow readings, or
- Normal spirometry, a FeNO level of 34 ppb or less and positive peak flow variability.

Do not rule out other diagnoses if symptom control continues to remain poor after treatment. Review the diagnosis after 6 weeks by repeating any abnormal tests and reviewing symptoms.

Refer children and young people (aged 5 to 16) for specialist assessment if they have obstructive spirometry, negative bronchodilator reversibility and a FeNO level of 34 ppb or less.

Consider alternative diagnoses and referral for specialist assessment in children and young people (aged 5 to 16) if they have symptoms suggestive of asthma but normal spirometry, a FeNO level of 34 ppb or less and negative peak flow variability.

Diagnosis in Adults Aged 17 and Over

See also algorithm C in the original guideline document for objective tests in adults aged 17 and over.

Diagnose asthma in adults (aged 17 and over) if they have symptoms suggestive of asthma and:

- A FeNO level of 40 ppb or more with either positive bronchodilator reversibility or positive peak flow variability or bronchial hyperreactivity, or
- A FeNO level between 25 and 39 ppb and a positive bronchial challenge test, or
- Positive bronchodilator reversibility and positive peak flow variability irrespective of FeNO level.

Suspect asthma in adults (aged 17 and over) with symptoms suggestive of asthma, obstructive spirometry and:

- Negative bronchodilator reversibility, and either a FeNO level of 40 ppb or more, or a FeNO level between 25 and 39 ppb and positive peak flow variability, or
- Positive bronchodilator reversibility, a FeNO level between 25 and 39 ppb and negative peak flow variability.

Do not rule out other diagnoses if symptom control continues to remain poor after treatment. Review the diagnosis after 6 to 10 weeks by repeating spirometry and objective measures of asthma control and reviewing symptoms.

Consider alternative diagnoses, or referral for a second opinion, in adults (aged 17 and over) with symptoms suggestive of asthma and:

- A FeNO level below 40 ppb, normal spirometry and positive peak flow variability, or
- A FeNO level of 40 ppb or more but normal spirometry, negative peak flow variability, and negative bronchial challenge test, or
- Obstructive spirometry with bronchodilator reversibility, but a FeNO level below 25 ppb, and negative peak flow variability, or
- Positive peak flow variability but normal spirometry, a FeNO level below 40 ppb, and a negative bronchial challenge test, or
- Obstructive spirometry with negative bronchodilator reversibility, a FeNO level below 25 ppb, and negative peak flow variability (if measured).

Diagnosis in People Who Are Unable to Perform an Objective Test

For young children who cannot perform objective tests, see "Diagnosing Asthma in Young Children," above.

If an adult, young person or child with symptoms suggestive of asthma cannot perform a particular test, try to perform at least 2 other objective tests. Diagnose suspected asthma based on symptoms and any positive objective test results.

Good Clinical Practice in Asthma Diagnosis

Record the basis for a diagnosis of asthma in a single entry in the person's medical records, alongside the coded diagnostic entry.

Diagnostic Summary

The following algorithms have been produced that summarise clinical assessment and objective testing for asthma. Table 1 in the original guideline document summarises the objective test threshold levels.

Principles of Pharmacological Treatment

Take into account the possible reasons for uncontrolled asthma, before starting or adjusting medicines for asthma in adults, young people and children. These may include:

- Alternative diagnoses
- Lack of adherence
- Suboptimal inhaler technique
- Smoking (active or passive)
- Occupational exposures
- Psychosocial factors
- Seasonal or environmental factors

After starting or adjusting medicines for asthma, review the response to treatment in 4 to 8 weeks (see "Monitoring Asthma Control" below).

If inhaled corticosteroid (ICS) maintenance therapy is needed, offer regular daily ICS rather than intermittent or 'when required' ICS therapy.

Adjust the dose of ICS maintenance therapy over time, aiming for the lowest dose required for effective asthma control.

Ensure that a person with asthma can use their inhaler device:

- At any asthma review, either routine or unscheduled
- Whenever a new type of device is supplied

Pharmacological Treatment Pathway for Adults (Aged 17 and Over)

This section is for people with newly diagnosed asthma or asthma that is uncontrolled on their current treatment. Where the recommendations represent a change from traditional clinical practice, people whose asthma is well controlled on their current treatment should not have their treatment changed purely to follow this guidance.

Offer a short-acting $beta_2$ agonist (SABA) as reliever therapy to adults (aged 17 and over) with newly diagnosed asthma.

For adults (aged 17 and over) with asthma who have infrequent, short-lived wheeze and normal lung function, consider treatment with SABA reliever therapy alone.

Offer a low dose of an ICS as the first-line maintenance therapy to adults (aged 17 and over) with:

- Symptoms at presentation that clearly indicate the need for maintenance therapy (for example, asthma-related symptoms 3 times a week or more, or causing waking at night), or
- Asthma that is uncontrolled with a SABA alone.

If asthma is uncontrolled in adults (aged 17 and over) on a low dose of ICS as maintenance therapy, offer a leukotriene receptor antagonist (LTRA) in addition to the ICS and review the response to treatment in 4 to 8 weeks.

If asthma is uncontrolled in adults (aged 17 and over) on a low dose of ICS and an LTRA as maintenance therapy, offer a long-acting beta2 agonist (LABA) in combination with the ICS, and review LTRA treatment as follows:

- Discuss with the person whether or not to continue LTRA treatment
- Take into account the degree of response to LTRA treatment

If asthma is uncontrolled in adults (aged 17 and over) on a low dose of ICS and a LABA, with or without an LTRA, as maintenance therapy, offer to change the person's ICS and LABA maintenance therapy to a MART regimen with a low maintenance ICS dose.

If asthma is uncontrolled in adults (aged 17 and over) on a MART regimen with a low maintenance ICS

dose, with or without an LTRA, consider increasing the ICS to a moderate maintenance dose (either continuing on a MART regimen or changing to a fixed-dose of an ICS and a LABA, with a SABA as a reliever therapy).

If asthma is uncontrolled in adults (aged 17 and over) on a moderate maintenance ICS dose with a LABA (either as MART or a fixed-dose regimen), with or without an LTRA, consider:

- Increasing the ICS to a high maintenance dose (this should only be offered as part of a fixed-dose regimen, with a SABA used as a reliever therapy), or
- a trial of an additional drug (for example, a long-acting muscarinic receptor antagonist or theophylline), or
- Seeking advice from a healthcare professional with expertise in asthma.

Pharmacological Treatment Pathway for Children and Young People Aged 5 to 16

This section is for children and young people with newly diagnosed asthma or asthma that is uncontrolled on their current treatment. Where the recommendations represent a change from traditional clinical practice, children and young people whose asthma is well controlled on their current treatment should not have their treatment changed purely to follow guidance.

Offer a SABA as reliever therapy to children and young people (aged 5 to 16) with newly diagnosed asthma.

For children and young people (aged 5 to 16) with asthma who have infrequent, short-lived wheeze and normal lung function, consider treatment with SABA reliever therapy alone.

Offer a paediatric low dose of an ICS as the first-line maintenance therapy to children and young people (aged 5 to 16) with:

- Symptoms at presentation that clearly indicate the need for maintenance therapy (for example, asthma-related symptoms 3 times a week or more, or causing waking at night), or
- Asthma that is uncontrolled with a SABA alone.

If asthma is uncontrolled in children and young people (aged 5 to 16) on a paediatric low dose of ICS as maintenance therapy, consider an LTRA[4] in addition to the ICS and review the response to treatment in 4 to 8 weeks.

If asthma is uncontrolled in children and young people (aged 5 to 16) on a paediatric low dose of ICS and an LTRA as maintenance therapy, consider stopping the LTRA and starting a LABA[5] in combination with the ICS.

If asthma is uncontrolled in children and young people (aged 5 to 16) on a paediatric low dose of ICS and a LABA as maintenance therapy, consider changing their ICS and LABA maintenance therapy to a MART regimen[6] with a paediatric low maintenance ICS dose. Ensure that the child or young person is able to understand and comply with the MART regimen.

If asthma is uncontrolled in children and young people (aged 5 to 16) on a MART regimen[6] with a paediatric low maintenance ICS dose, consider increasing the ICS to a paediatric moderate maintenance dose (either continuing on a MART regimen or changing to a fixed-dose of an ICS and a LABA, with a SABA as a reliever therapy).

If asthma is uncontrolled in children and young people (aged 5 to 16) on a paediatric moderate maintenance ICS dose with LABA (either as MART[6] or a fixed-dose regimen), consider seeking advice from a healthcare professional with expertise in asthma and consider either:

- Increasing the ICS dose to paediatric high maintenance dose (only as part of a fixed-dose regimen, with a SABA used as a reliever therapy), or
- A trial of an additional drug (for example, theophylline).

Pharmacological Treatment Pathway for Children Under 5

It can be difficult to confirm asthma diagnosis in young children, therefore these recommendations apply to children with suspected or confirmed asthma. Asthma diagnosis should be confirmed when the child is able to undergo objective tests (see "Diagnosing Asthma in Young Children," above).

This section is for children under 5 with newly suspected or confirmed asthma, or with asthma symptoms that are uncontrolled on their current treatment. Where the recommendations represent a change from traditional clinical practice, children whose asthma is well controlled on their current treatment should not have their treatment changed purely to follow this guidance.

Offer a SABA as reliever therapy to children under 5 with suspected asthma. This should be used for symptom relief alongside all maintenance therapy.

Consider an 8-week trial of a paediatric moderate dose of an ICS in children under 5 with:

- Symptoms at presentation that clearly indicate the need for maintenance therapy (for example, asthma-related symptoms 3 times a week or more, or causing waking at night), or
- Suspected asthma that is uncontrolled with a SABA alone.

After 8 weeks, stop ICS treatment and continue to monitor the child's symptoms:

- If symptoms did not resolve during the trial period, review whether an alternative diagnosis is likely
- If symptoms resolved then reoccurred within 4 weeks of stopping ICS treatment, restart the ICS at a paediatric low dose as first-line maintenance therapy
- If symptoms resolved but reoccurred beyond 4 weeks after stopping ICS treatment, repeat the 8-week trial of a paediatric moderate dose of ICS

If suspected asthma is uncontrolled in children under 5 on a paediatric low dose of ICS as maintenance therapy, consider an LTRA[7] in addition to the ICS.

If suspected asthma is uncontrolled in children under 5 on a paediatric low dose of ICS and an LTRA as maintenance therapy, stop the LTRA and refer the child to a healthcare professional with expertise in asthma for further investigation and management.

Adherence

For guidance on managing non-adherence to medicines in people with asthma, see the NICE guideline on medicines adherence .

Self-management

Offer an asthma self-management programme, comprising a written personalised action plan and education, to adults, young people and children aged 5 and over with a diagnosis of asthma (and their families or carers if appropriate).

Consider an asthma self-management programme, comprising a written personalised action plan and education, for the families or carers of children under 5 with suspected or confirmed asthma.

Increasing ICS Treatment Within a Self-management Programme

Within a self-management programme, offer an increased dose of ICS for 7 days to adults (aged 17 and over) who are using an ICS in a single inhaler, when asthma control deteriorates. Clearly outline in the person's asthma action plan how and when to do this, and what to do if symptoms do not improve. When increasing ICS treatment:

- Consider quadrupling the regular ICS dose
- Do not exceed the maximum licensed daily dose

Within a self-management programme, consider an increased dose of ICS for 7 days for children and

young people (aged 5 to 16) who are using an ICS in a single inhaler, when asthma control deteriorates. Clearly outline in the person's asthma action plan how and when to do this, and what to do if symptoms do not improve. When increasing ICS treatment:

- Consider quadrupling the regular ICS dose
- Do not exceed the maximum licensed daily dose

Decreasing Maintenance Therapy

Consider decreasing maintenance therapy when a person's asthma has been controlled with their current maintenance therapy for at least 3 months.

Discuss with the person (or their family or carer if appropriate) the potential risks and benefits of decreasing maintenance therapy.

When reducing maintenance therapy:

- Stop or reduce dose of medicines in an order that takes into account the clinical effectiveness when introduced, side effects and the person's preference
- Only consider stopping ICS treatment completely for people who are using low dose ICS alone as maintenance therapy and are symptom free

Agree with the person (or their family or carer if appropriate) how the effects of decreasing maintenance therapy will be monitored and reviewed, including self-monitoring and a follow-up with a healthcare professional.

Review and update the person's asthma action plan when decreasing maintenance therapy.

Risk Stratification

Consider using risk stratification to identify people with asthma who are at increased risk of poor outcomes, and use this information to optimise their care. Base risk stratification on factors such as non-adherence to asthma medicines, psychosocial problems and repeated episodes of unscheduled care for asthma.

Monitoring Asthma Control

Monitor asthma control at every review. If control is suboptimal:

- Confirm the person's adherence to prescribed treatment in line with the recommendations on assessing adherence in the NICE guideline on medicines adherence
- Review the person's inhaler technique
- Review if treatment needs to be changed
- Ask about occupational asthma (see "Self-management" above) and/or other triggers, if relevant

Consider using a validated questionnaire (for example, the Asthma Control Questionnaire or Asthma Control Test) to monitor asthma control in adults (aged 17 and over).

Monitor asthma control at each review in adults, young people and children aged 5 and over using either spirometry or peak flow variability testing.

Do not routinely use FeNO to monitor asthma control.

Consider FeNO measurement as an option to support asthma management in people who are symptomatic despite using inhaled corticosteroids. (This recommendation is from the NICE diagnostics guidance on measuring fractional exhaled nitric oxide concentration in asthma.)

Do not use challenge testing to monitor asthma control.

Observe and give advice on the person's inhaler technique:

At every consultation relating to an asthma attack, in all care settings
When there is deterioration in asthma control
When the inhaler device is changed
At every annual review
If the person asks for it to be checked

Footnotes

[1]'Holiday' here means any longer time away from work than usual breaks at weekends or between shifts.

[2]Children at the lower end of the age range may not be able to do the FeNO test adequately. In these cases, apply the principles in "Diagnosing Asthma in Young Children."

[3]At the time of publication (November 2017), histamine and methacholine did not have UK marketing authorisation for this use. The healthcare professional should follow relevant professional guidance, taking full responsibility for the decision to use this test. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[4]At the time of publication (November 2017), not all LTRAs have a UK marketing authorisation for use in children and young people aged under 18 for this indication.

[5]At the time of publication (November 2017), not all LABAs have a UK marketing authorisation for use in children and young people aged under 18 for this indication.

[6]At the time of publication (November 2017), MART regimens did not have a UK marketing authorisation for use in children and young people (aged under 12) for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[7]At the time of publication (November 2017), not all LTRAs have a UK marketing authorisation for use in children and young people aged under 18 for this indication.

Definitions

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee (GC) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GC is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.

Interventions That Must (or Must Not) Be Used

The GC usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally they use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GC uses 'offer' (and similar words such as 'refer' or 'advise') when they are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. They use similar forms of words (for example, 'Do not offer…') when they are confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GC uses 'consider' when they are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should

spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

The following are provided on the National Institute for Health and Care Excellence (NICE) Web site :

- Algorithm A: Initial clinical assessment for adults, young people and children with suspected asthma
- Algorithm B: Objective tests for asthma in children and young people aged 5 to 16
- Algorithm C: Objective tests for asthma in adults aged 17 and over
- Algorithm D: Pharmacological treatment of chronic asthma in children under 5
- Algorithm E: Pharmacological treatment of chronic asthma in children and young people aged 5 to 16
- Algorithm F: Pharmacological treatment of chronic asthma in adults aged 17 and over

In addition, a NICE pathway titled "Asthma overview" is provided on the NICE Web site .

Scope

Disease/Condition(s)

Asthma

Note: The guideline does not cover managing severe, difficult-to-control asthma or acute asthma attacks.

Guideline Category

Diagnosis

Evaluation

Management

Clinical Specialty

Allergy and Immunology

Family Practice

Internal Medicine

Pulmonary Medicine

Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Patients

Physician Assistants

Physicians

Respiratory Care Practitioners

Guideline Objective(s)

To improve the accuracy of diagnosis, help people to control their asthma and reduce the risk of asthma attacks

Target Population

Adults, children and young people who are being investigated for suspected asthma, or who have been diagnosed with asthma and are having their condition monitored

Note: Specific consideration for asthma diagnosis and management is given to subgroups based on age, broadly divided into younger children, older children, and older people (aged over 75 years). Specific consideration for chronic asthma management will be given based on age, with proposed banding of children under 5 years; children aged 5 to 16; and adults and young people over 16 years of age.

Interventions and Practices Considered

1. Initial clinical assessment
    - Clinical history
    - Physical examination
    - Initial treatment and objective tests for acute symptoms at presentation
    - Testing for asthma
    - Assessment for occupational asthma
2. Diagnosing asthma in young children: observation and clinical judgement
3. Objective tests for diagnosing asthma in adults, young people, and children aged 5 and over
    - Diagnostic hubs
    - Airway inflammation measures (i.e., fractional exhaled nitric oxide)
    - Lung function tests
    - Airway hyperreactivity measures
4. Pharmacological treatment
    - Short-acting $beta_2$ agonist (SABA)
    - Inhaled corticosteroid (ICS)
    - Maintenance and reliever therapy (MART) (combined ICS and LABA treatment)
    - Leukotriene receptor antagonist (LTRA)
    - Long-acting $beta_2$ agonist (LABA)
5. Self-management, including increasing ICS treatment within a self-management program
6. Decreasing maintenance therapy
7. Risk stratification for patients
8. Monitoring asthma control

Major Outcomes Considered

- Diagnostic accuracy (sensitivity and specificity of diagnostic tests)
- Unscheduled healthcare utilisation (UHU)
- Exacerbations (defined as need for course of oral steroids)
- Asthma control questionnaires
- Adherence
- Mortality
- Quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Guideline Centre on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full versions of this guidance and related appendices.

Asthma: Diagnosis and Monitoring of Asthma in Adults, Children and Young People

Review questions were developed in a PICO (population, intervention, comparison and outcome) framework (patient, intervention, comparison and outcome) for intervention reviews in a framework of population, index tests, reference standard and target condition for reviews of diagnostic test accuracy; and using population, presence or absence of factors under investigation (for example prognostic factors) and outcomes for prognostic reviews.

This use of a framework guided the literature searching process, critical appraisal and synthesis of evidence, and facilitated the development of recommendations by the Guideline Committee (GC). The review questions were drafted by the NGC technical team and refined and validated by the GC. The questions were based on the key clinical areas identified in the scope (Appendix A).

A total of 23 review questions were identified.

Full literature searches, critical appraisals and evidence reviews were completed for all the specified review questions.

Searching for Evidence

Clinical Literature Search

Systematic literature searches were undertaken to systematically identify all published clinical evidence relevant to the review questions. Searches were undertaken according to the parameters stipulated within *The guidelines manual* 2012. Databases were searched using relevant medical subject headings, free-text terms and study-type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English. All searches were conducted in MEDLINE, EMBASE, and The Cochrane Library. All searches were updated on 1 October 2014. No papers published after this date were considered.

Search strategies were quality assured by cross-checking reference lists of highly relevant papers, analysing search strategies in other systematic reviews, and asking GC members to highlight any additional studies. The questions, the study types applied, the databases searched and the years covered can be found in Appendix F.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the inclusion criteria.

Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting a broad

search relating to asthma in the NHS Economic Evaluation Database (NHS EED), the Health Technology Assessment database (HTA) and the Health Economic Evaluations Database (HEED) with no date restrictions. Additionally, the search was run on MEDLINE and EMBASE using a specific economic filter, from 2012 to ensure recent publications that had not yet been indexed by the economic databases were identified. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English.

The health economic search strategies are included in Appendix F. All searches were updated on 1 October 2014. No papers published after this date were considered.

Updated Searches 2017

The systematic literature searches for all the review questions were rerun in March 2017. The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the protocol inclusion criteria for appropriate review questions and in total 9 studies were identified. Appendix R: 'Summary of evidence from 2017 update of Asthma: diagnosis and monitoring' outlines the studies that were identified and the questions and recommendations they were relevant to. The update summary details the impact the identified evidence has on the guideline recommendations; the GC considered that none of the studies had a significant impact on the evidence base and would not lead to a change in recommendations. The studies were therefore not used to update the guideline evidence base.

See Section 3.4.1 in the full version of the guideline for inclusion and exclusion criteria.

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Developing the Review Questions and Outcomes

Review questions were developed using a PICO framework for intervention reviews; using a framework of population, index tests, reference standard and target condition for diagnostic test accuracy reviews; and using population, presence or absence of factors under investigation (for example prognostic factors) and outcomes for prognostic reviews.

This use of a framework guided the literature searching process, critical appraisal and synthesis of evidence, and facilitated the development of recommendations by the committee. The review questions were drafted by the NGC technical team and refined and validated by the committee. The questions were based on the key clinical areas identified in the scope (Appendix A).

A total of 12 review questions were identified.

Full literature searches, critical appraisals and evidence reviews were completed for all the specified review questions.

Minimum trial durations were specified for each outcome. Minimum durations were chosen by the committee as the first time points for which a clinically meaningful difference in the outcome would be observable. Rarer outcomes such as mortality and severe exacerbations therefore had longer minimum durations than more responsive outcomes like lung function and asthma control.

Searching for Evidence

Clinical Literature Search

Systematic literature searches were undertaken to identify all published clinical evidence relevant to the review questions. Searches were undertaken according to the parameters stipulated within the NICE guidelines manual 2014. Databases were searched using relevant medical subject headings, free-text terms and study-type filters where appropriate. Where possible, searches were restricted to papers published in English. Studies published in languages other than English were not reviewed. All searches were conducted in Medline, EMBASE, and The Cochrane Library. Additional subject- specific databases were used for some questions: Allied and Complementary Medicine (AMED). All searches were updated on

12 September 2016. No papers published after this date were considered.

Search strategies were quality assured by cross-checking reference lists of highly relevant papers, analysing search strategies in other systematic reviews, and asking committee members to highlight any additional studies. Searches were quality assured by a second information scientist before being run. The questions, the study types applied, the databases searched and the years covered can be found in Appendix G.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the inclusion criteria.

During the scoping stage, a search was conducted for guidelines and reports on the Web sites listed below from organisations relevant to the topic.

Guidelines International Network database (www.g-i-n.net)
National Guideline Clearinghouse (www.guideline.gov)
National Institute for Health and Care Excellence (NICE) (www.nice.org.uk)
National Institutes of Health Consensus Development Program (consensus.nih.gov)
NHS Evidence Search (www.evidence.nhs.uk).

All references sent by stakeholders were considered. Searching for unpublished literature was not undertaken. The National Guideline Centre and NICE do not have access to drug manufacturers' unpublished clinical trial results, so the clinical evidence considered by the committee for pharmaceutical interventions may be different from that considered by the UK's Medicines and Healthcare products Regulatory Agency (MHRA) and European Medicines Agency for the purposes of licensing and safety regulation.

Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting a broad search relating to asthma in the NHS EED, the HTA database with no date restrictions (NHS EED ceased to be updated after March 2015). Additionally, the search was run on Medline and EMBASE using a health economic filter, from January 2014, to ensure recent publications that had not yet been indexed by the economic databases were identified. Where possible, searches were restricted to papers published in English. Studies published in languages other than English were not reviewed.

The health economic search strategies are included in Appendix G. All searches were updated on 12 September 2016. No papers published after this date were considered.

See Section 4.3.1 in the full version of the guideline for inclusion and exclusion criteria.

Number of Source Documents

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See Appendix D, "Clinical article selection" and Appendix E, "Economic article selection" (see the "Availability of Companion Documents" field) for information on results of literature searches and the number of included and excluded studies for each review question.

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See Appendix E, "Clinical article selection" and Appendix F, "Economic article selection" (see the "Availability of Companion Documents" field) for information on results of literature searches and the number of included and excluded studies for each review question.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Guideline Centre on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full versions of this guidance and related appendices.

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Evidence of Effectiveness

The evidence was reviewed following the steps shown schematically in Figure 1 in the full version of the guideline:

Relevant studies were critically appraised using the appropriate checklist as specified in The guidelines manual (see the "Availability of Companion Documents" field). For diagnostic questions, the quality assessment tool for diagnostic accuracy studies (QUADAS)-2 checklist was followed (http://www.bris.ac.uk/quadas/quadas-2/).
Key information was extracted on the study's methods, PICO (population, intervention, comparison and outcome) factors and results. These were presented in summary tables (in each review chapter) and evidence tables (in Appendix G).
Summaries of evidence were generated by outcome (included in the relevant review chapters) and were presented in GC meetings:

- Randomised studies: data were meta-analysed where appropriate and reported in Grading of Recommendations Assessment, Development and Evaluation (GRADE) profiles (for intervention reviews).
- Observational studies: data were presented as a range of values in GRADE profiles.
- Prognostic studies: data were presented as a range of values, usually in terms of the relative effect as reported by the authors.
- Diagnostic studies were presented as measures of diagnostic test accuracy (sensitivity, specificity, positive and negative predictive value). Coupled values of sensitivity and specificity were summarised in receiver operating curves (ROCs) to investigate heterogeneity more

effectively, where evidence was available from five or more studies for any one index test. A meta-analysis of the summary operating point (i.e., summary values for sensitivity and specificity) could not be conducted for any of the index tests, because the studies reported data at various thresholds and because data at any one threshold were not available from five or more studies.

Qualitative studies: each study was summarised in a table where possible, otherwise presented in a narrative.

A 20% sample of each of the above stages of the reviewing process was quality assured by a second reviewer to eliminate any potential of reviewer bias or error.

Methods of Combining Clinical Studies

Refer to Section 3.4.2 in the full version of the guideline for data synthesis for intervention reviews and for diagnostic test accuracy review.

Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included randomized controlled trials (RCTs) and, where appropriate, observational studies were evaluated and presented using an adaptation of the 'GRADE toolbox' developed by the international GRADE working group (http://www.gradeworkinggroup.org/). The software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking into account individual study quality factors and the meta-analysis results. Results were presented in GRADE profiles ('GRADE tables'), which consist of 2 sections: the 'Clinical evidence profile' table includes details of the quality assessment while the 'Clinical evidence summary of findings' table includes pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate summary measures and measures of dispersion (such as mean and standard deviation or median and range) for continuous outcomes and frequency of events (n/N: the sum across studies of the number of patients with events divided by sum of the number of completers) for binary outcomes. Reporting or publication bias was only taken into consideration in the quality assessment and included in the 'Clinical evidence profile' table if it was apparent.

The evidence for each outcome was examined separately for the quality elements listed and defined in Table 2 in the full version of the guideline. Each element was graded using the quality levels listed in Table 3. The main criteria considered in the rating of these elements are discussed below (see Section 3.4.5, Grading of evidence, in the full version of the guideline). Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall assessment for each outcome (see the "Rating Scheme for the Strength of the Evidence" field).

The GRADE toolbox is currently designed only for randomised trials and observational studies but we adapted the quality assessment elements and outcome presentation for diagnostic accuracy studies.

Grading the Quality of Clinical Evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

A quality rating was assigned, based on the study design. RCTs start as High, observational studies as Low, and uncontrolled case series as Low or Very low.

The rating was then downgraded for the specified criteria: risk of bias (study limitations), inconsistency, indirectness, imprecision and publication bias. These criteria are detailed below.

Evidence from observational studies (which had not previously been downgraded) was upgraded if there was: a large magnitude of effect, a dose–response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect.

Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down by 1 or 2 points respectively.

The downgraded or upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as High and the overall quality became Moderate, Low or Very low if 1, 2 or 3 points were deducted respectively.
The reasons or criteria used for downgrading were specified in the footnotes.

The details of the criteria used for each of the main quality elements are discussed further in the Sections 3.4.6 to 3.4.9 in the full version of the guideline.

Assessing Clinical Importance

The GC assessed the evidence by outcome in order to determine if there was, or potentially was, a clinically important benefit, a clinically important harm or no clinically important difference between interventions. To facilitate this, binary outcomes were converted into absolute risk differences (ARDs) using GRADEpro software: the median control group risk across studies was used to calculate the ARD and its 95% confidence interval (CI) from the pooled risk ratio.

The assessment of benefit, harm, or no benefit or harm was based on the point estimate of absolute effect for intervention studies which was standardised across the reviews. The GC considered for most of the outcomes in the intervention reviews that if at least 100 participants per 1000 (10%) achieved (if positive) the outcome of interest in the intervention group compared to the comparison group then this intervention would be considered beneficial. The same point estimate but in the opposite direction would apply if the outcome was negative.

This assessment was carried out by the GC for each critical outcome, and an evidence summary table was produced to compile the GC's assessments of clinical importance per outcome, alongside the evidence quality and the uncertainty in the effect estimate (imprecision).

Evidence Statements

Evidence statements are summary statements that are presented after the GRADE profiles, summarising the key features of the clinical effectiveness evidence presented. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect. The evidence statements are presented by outcome and encompass the following key features of the evidence:

The number of studies and the number of participants for a particular outcome
A brief description of the participants
An indication of the direction of effect (if one treatment is beneficial or harmful compared to the other, or whether there is no difference between the 2 tested treatments)
A description of the overall quality of evidence (GRADE overall quality).

Evidence of Cost-effectiveness

Refer to Section 3.5 in the full version of the guideline for analysis of evidence of cost-effectiveness.

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Analysing Evidence of Effectiveness

Research fellows conducted the tasks listed below, which are described in further detail in the rest of this section:

Critically appraised relevant studies using the appropriate study design checklist as specified in the NICE guidelines manual. Prognostic or qualitative studies were critically appraised using National Guideline Centre checklists.
Extracted key information about interventional study methods and results using 'Evibase', the National Guideline Centre's purpose-built software. Evibase produces summary evidence tables, including critical appraisal ratings. Key information about non-interventional study methods and results was manually extracted onto standard evidence tables and critically appraised separately (evidence tables are included in Appendix H).

Generated summaries of the evidence by outcome. Outcome data were combined, analysed and reported according to study design:

- Randomised data were meta-analysed where appropriate and reported in GRADE profile tables.
- Prognostic data were meta-analysed where appropriate and reported in GRADE profile tables.

A sample of a minimum of 10% of the abstract lists of the first 3 sifts by new reviewers and those for complex review questions (for example, prognostic reviews) were double-sifted by a senior research fellow and any discrepancies were rectified. All of the evidence reviews were quality assured by a senior research fellow. This included checking:

- Papers were included or excluded appropriately
- A sample of the data extractions
- Correct methods were used to synthesise data
- A sample of the risk of bias assessments.

Methods of Combining Clinical Studies

Refer to Section 3.3.3 in the full version of the guideline for data synthesis for intervention reviews and for prognostic factor reviews.

Appraising the Quality of Evidence by Outcomes

Intervention Reviews

The evidence for outcomes from the included RCTs and, where appropriate, non-randomised intervention studies, were evaluated and presented using an adaptation of the 'GRADE toolbox' developed by the international GRADE working group (http://www.gradeworkinggroup.org/). The software (GRADEpro) developed by the GRADE working group was used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results.

Each outcome was first examined for each of the quality elements listed and defined in Table 4 in the full version of the guideline.

Refer to Sections 4.3.4.1.1 to 4.3.4.1.5 for additional information, including overall grading of the quality of clinical evidence.

Prognostic Reviews

The quality of evidence for prognostic studies was evaluated according to the criteria given in Table 7 in the full version of the guideline. If data were meta-analysed, the quality for pooled studies was presented. If the data were not pooled, then a quality rating was presented for each study.

Refer to Sections 4.3.4.2.1 to 4.3.4.2.3 in the full guideline for additional information, including overall grading.

Assessing Clinical Importance

The committee assessed the evidence by outcome in order to determine if there was, or potentially was, a clinically important benefit, a clinically important harm or no clinically important difference between interventions. To facilitate this, binary outcomes were converted into absolute risk differences (ARDs) using GRADEpro software: the median control group risk across studies was used to calculate the ARD and its 95% CI from the pooled risk ratio.

The assessment of clinical benefit, harm, or no benefit or harm was based on the point estimate of absolute effect for intervention studies, which was standardised across the reviews. The committee considered for most of the outcomes in the intervention reviews that if at least 10 more participants per 1000 (1%) achieved the outcome of interest in the intervention group compared to the comparison group for a positive outcome then this intervention was considered beneficial. The same point estimate but in the opposite direction applied for a negative outcome. For minor adverse events 50 events or more per 1000 (5%) represented clinical harm. For continuous outcomes if the mean difference was greater than the minimally important difference (MID) then this represented a clinical benefit or harm. For outcomes

such as mortality any reduction or increase was considered to be clinically important.

This assessment was carried out by the committee for each critical outcome, and an evidence summary table was produced to compile the committee's assessments of clinical importance per outcome, alongside the evidence quality and the uncertainty in the effect estimate (imprecision).

Clinical Evidence Statements

Clinical evidence statements are summary statements that are included in each review chapter, and which summarise the key features of the clinical effectiveness evidence presented. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect. The evidence statements are presented by outcome and encompass the following key features of the evidence:

The number of studies and the number of participants for a particular outcome.
An indication of the direction of clinical importance (if one treatment is beneficial or harmful compared to the other, or whether there is no difference between the 2 tested treatments).
A description of the overall quality of the evidence (GRADE overall quality).

Analysing Evidence of Cost-effectiveness

Refer to Section 4.4 in the full version of the guideline for analysis of evidence of cost-effectiveness.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Guideline Centre on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full versions of this guidance and related appendices.

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Who Developed This Guideline?

A multidisciplinary Guideline Committee (GC) comprising health professionals and researches as well as lay members developed this guideline.

NICE funds the National Guideline Centre and thus supported the development of this guideline. The GC was convened by the National Guideline Centre and chaired by Dr. Andrew Menzies-Gow in accordance with guidance from NICE. The group met every 5 to 6 weeks during the development of the guideline.

Staff from the NGC provided methodological support and guidance for the development process. The team working on the guideline included a project manager, systematic reviewers, health economists and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate and drafted the guideline in collaboration with the GC.

Developing Recommendations

Over the course of the guideline development process, the GC was presented with:

Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendices H and I.
Summary of clinical and economic evidence and quality (as presented in Chapters 6 to 30).
Forest plots and summary ROC curves (Appendix J).

A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (Appendix M).

Recommendations were drafted on the basis of the GC interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. This was either done formally in an economic model, or informally. Firstly, the net benefit over harm (clinical effectiveness) was considered, focusing on the critical outcomes. When this was done informally, the GC took into account the clinical benefits and harms when one intervention was compared with another. The assessment of net benefit was moderated by the importance placed on the outcomes (the GC's values and preferences), and the confidence the GC had in the evidence (evidence quality). Secondly, it was assessed whether the net benefit justified any differences in costs.

When clinical and economic evidence was of poor quality, conflicting or absent, the GC drafted recommendations based on their expert opinion. The considerations for making consensus-based recommendations include the balance between potential harms and benefits, the economic costs compared to the economic benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. The consensus recommendations were agreed through discussions in the GC. The GC also considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation (see Section 3.6.1 in the full version of the guideline).

The wording of recommendations was agreed by the GC and focused on the following factors:

The actions health professionals need to take.
The information readers need to know.
The strength of the recommendation (for example the word 'offer' was used for strong recommendations and 'consider' for weak recommendations).
The involvement of patients (and their carers if needed) in decisions on treatment and care.
Consistency with NICE's standard advice on recommendations about drugs, waiting times and ineffective interventions.

The main considerations specific to each recommendation are outlined in the 'Recommendations and link to evidence' sections within each chapter in the full version of the guideline.

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Who Developed This Guideline?

A multidisciplinary Guideline Committee ('the committee') comprising health professionals and researchers as well as lay members developed this guideline.

NICE funds the National Guideline Centre and thus supported the development of this guideline. The committee was convened by the National Guideline Centre and chaired by Dr John Alexander in accordance with guidance from NICE. The group met approximately every 6 to 8 weeks during the development of the guideline.

Staff from the National Guideline Centre provided methodological support and guidance for the development process. The team working on the guideline included a project manager, systematic reviewers (research fellows), health economists and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate and drafted the guideline in collaboration with the committee.

Developing Recommendations

Over the course of the guideline development process, the committee was presented with:

Evidence tables of the clinical and health economic evidence reviewed from the literature. All evidence tables are in Appendices H and I.
Summaries of clinical and health economic evidence and quality (as presented in Chapters 5–14).

Forest plots (Appendix K).
A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (Appendix N).

Recommendations were drafted on the basis of the committee's interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. This was either done formally in an economic model, or informally. Firstly, the net clinical benefit over harm (clinical effectiveness) was considered, focusing on the critical outcomes. When this was done informally, the committee took into account the clinical benefits and harms when one intervention was compared with another. The assessment of net clinical benefit was moderated by the importance placed on the outcomes (the committee's values and preferences), and the confidence the committee had in the evidence (evidence quality). Secondly, the committee assessed whether the net clinical benefit justified any differences in costs between the alternative interventions.

When clinical and health economic evidence was of poor quality, conflicting or absent, the committee drafted recommendations based on its expert opinion. The considerations for making consensus-based recommendations include the balance between potential harms and benefits, the economic costs compared to the economic benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. The consensus recommendations were agreed through discussions in the committee. The committee also considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation (see Section 4.5.1 below).

The committee considered the appropriate 'strength' of each recommendation. This takes into account the quality of the evidence but is conceptually different. Some recommendations are 'strong' in that the committee believes that the vast majority of healthcare and other professionals and patients would choose a particular intervention if they considered the evidence in the same way that the committee has. This is generally the case if the benefits clearly outweigh the harms for most people and the intervention is likely to be cost-effective. However, there is often a closer balance between benefits and harms, and some patients would not choose an intervention whereas others would. This may happen, for example, if some patients are particularly averse to some side effect and others are not. In these circumstances the recommendation is generally weaker, although it may be possible to make stronger recommendations about specific groups of patients.

The committee focused on the following factors in agreeing the wording of the recommendations:

The actions health professionals need to take.
The information readers need to know.
The strength of the recommendation (for example the word 'offer' was used for strong recommendations and 'consider' for weaker recommendations).
The involvement of patients (and their carers if needed) in decisions on treatment and care.
Consistency with NICE's standard advice on recommendations about drugs, waiting times and ineffective interventions (see Section 9.2 in the 2014 NICE guidelines manual [see the "Availability of Companion Documents" field])

The main considerations specific to each recommendation are outlined in the 'Recommendations and link to evidence' sections within each chapter of the full version of the guideline.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee (GC) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GC is confident that, given the information it has looked at, most patients would choose the intervention. The wording

used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, National Institute for Health and Care Excellence (NICE) expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.

Interventions That Must (or Must Not) Be Used

The GC usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally they use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GC uses 'offer' (and similar words such as 'refer' or 'advise') when they are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. They use similar forms of words (for example, 'Do not offer…') when they are confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GC uses 'consider' when they are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

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Refer to Appendix M (see the "Availability of Companion Documents" field) for the full health economics report.

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Refer to Appendix N (see the "Availability of Companion Documents" field) for the full health economics report.

Method of Guideline Validation

Clinical Validation-Pilot Testing

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

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Validation Process

A draft of this guideline was subject to a 6-week public consultation during January-February 2015 as part of the quality assurance and peer review of the document. During consultation, some stakeholders suggested that a large investment in training and equipment would be needed to bring current practice in line with the guideline's diagnostic test recommendations, and that this was likely to be a major barrier

to implementation. The concerns centred around the need for objective tests to confirm the diagnosis, whereas traditional management had relied in many cases on clinical history supplemented by examination findings and a trial of asthma treatment. This applied to some extent to all the objective tests covered in the draft guideline, but pre-eminently to the use of fractional exhaled nitric oxide (FeNO) testing since this would be completely new to virtually every primary care group in England & Wales.

Guideline development was therefore paused in August 2015 to allow additional time to work with primary care professionals to assess the feasibility of adopting the diagnostic recommendations. An asthma feasibility project team was formed within the National Institute for Health and Care Excellence (NICE) Adoption and Impact team to work with 7 primary care sites across England, each of which agreed to implement the revised diagnostic recommendations and algorithms. The 7 sites were chosen to represent a cross-section (albeit small) of practices across the country with variation in size, geographical site and socio-economic profile of their patient lists. Outcome data was collected during a 6-month period May to October 2016. Further detail of the methods of this study, and its findings, are given in Appendix Q of this guideline (see the "Availability of Companion Documents" field).

The conclusions were important in determining the final recommendations in this guidance and are referred to in the relevant Linking Evidence to Recommendations (LETR) sections in addition to the consideration of the standard evidence sources.

The guideline, including some of the diagnostic recommendations and the associated algorithms, was amended in the light of the results of the feasibility study. This amended guidance was subject to a second period of consultation in July 2017.

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Validation Process

This guidance was subject to a 6-week public consultation and feedback as part of the quality assurance and peer review of the document. All comments received from registered stakeholders were responded to in turn and posted on the NICE Web site.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

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For monitoring reviews in this guideline, parallel randomised controlled trials (RCTs) were included because they are considered the most robust type of study design that could produce an unbiased estimate of the monitoring intervention effects. Crossover RCTs were not appropriate for the monitoring reviews due to the nature of the intervention, adjustment of treatment based on monitoring. Please refer to Appendix C (see the "Availability of Companion Documents" field) for full details on the study design of studies selected for each review question.

For diagnostic reviews, cross-sectional and retrospective studies were included. Case–control studies were not included for reviews of diagnostic test accuracy.

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Randomised trials, non-randomised intervention studies, and other observational studies (including diagnostic or prognostic studies) were included in the evidence reviews as appropriate.

For most intervention reviews in this guideline, parallel RCTs were included because they are considered the most robust type of study design that can produce an unbiased estimate of the intervention effects. Crossover RCTs were not appropriate for the questions on long-term preventers, adherence or self-management as the interventions in question would be likely to have a long-term effect that would

confound comparisons. If non-randomised intervention studies were considered appropriate for inclusion (for example, where no randomised evidence was available for critical outcomes) the committee stated a priori in the protocol that either certain identified variables must be equivalent at baseline or else the analysis had to adjust for any baseline differences. If the study did not fulfil either criterion it was excluded. Please refer to the review protocols in Appendix C (see the "Availability of Companion Documents" field) for full details on the study design of studies selected for each review question.

Where data from non-randomised studies were included, the results for each outcome were presented separately for each study or meta-analysed if appropriate.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Adherence to regular treatment reduces the risk of significant asthma attacks in most people with asthma.
- As occupational asthma is the only potentially curable type of asthma, there are considerable health benefits associated with the correct diagnosis of this type of asthma: people are able to eliminate the source of asthma, may return to a normal quality of life, and unnecessary treatment is averted.

Refer to the "Trade-off between benefits and harms" sections in the full versions of the guideline (see the "Availability of Companion Documents" field) for details about benefits of specific interventions.

Potential Harms

- False-positive and false-negative results of diagnostic testing
- Although inhaled corticosteroids (ICSs) are generally well tolerated they can have side effects, and they commit the person with asthma to taking an inhaler regularly, usually twice a day. Daily ICS use is associated with infection and adrenal insufficiency.

Refer to the "Trade-off between benefits and harms" sections in the full versions of the guideline (see the "Availability of Companion Documents" field) for details about potential harms of specific interventions.

Contraindications

Contraindications

The contraindications for spirometry should be considered (e.g., recent myocardial infarction [MI], recent eye surgery, etc.) when testing lung function.

Qualifying Statements

Qualifying Statements

- The recommendations in this guideline represent the view of the National Institute of Health and Care Excellence (NICE), arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people

using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

- Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.
- Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Implementation of the Guideline

Description of Implementation Strategy

Putting This Guideline into Practice

The National Institute for Health and Care Excellence (NICE) has produced tools and resources to help put this guideline into practice (see also the "Availability of Companion Documents" field).

Putting recommendations into practice can take time. How long may vary from guideline to guideline, and depends on how much change in practice or services is needed. Implementing change is most effective when aligned with local priorities.

Changes recommended for clinical practice that can be done quickly – like changes in prescribing practice – should be shared quickly. This is because healthcare professionals should use guidelines to guide their work – as is required by professional regulating bodies such as the General Medical and Nursing and Midwifery Councils.

Changes should be implemented as soon as possible, unless there is a good reason for not doing so (for example, if it would be better value for money if a package of recommendations were all implemented at once).

Different organisations may need different approaches to implementation, depending on their size and function. Sometimes individual practitioners may be able to respond to recommendations to improve their practice more quickly than large organisations.

Here are some pointers to help organisations put NICE guidelines into practice:

Raise awareness through routine communication channels, such as email or newsletters, regular meetings, internal staff briefings and other communications with all relevant partner organisations.
Identify things staff can include in their own practice straight away.
Identify a lead with an interest in the topic to champion the guideline and motivate others to support its use and make service changes, and to find out any significant issues locally.
Carry out a baseline assessment against the recommendations to find out whether there are gaps in current service provision.
Think about what data you need to measure improvement and plan how you will collect it. You may want to work with other health and social care organisations and specialist groups to compare current practice with the recommendations. This may also help identify local issues that will slow or prevent implementation.
Develop an action plan, with the steps needed to put the guideline into practice, and make sure it is ready as soon as possible. Big, complex changes may take longer to implement, but some may be

quick and easy to do. An action plan will help in both cases.

For very big changes include milestones and a business case, which will set out additional costs, savings and possible areas for disinvestment. A small project group could develop the action plan. The group might include the guideline champion, a senior organisational sponsor, staff involved in the associated services, finance and information professionals.

Implement the action plan with oversight from the lead and the project group. Big projects may also need project management support.

Review and monitor how well the guideline is being implemented through the project group. Share progress with those involved in making improvements, as well as relevant boards and local partners.

NICE provides a comprehensive programme of support and resources to maximise uptake and use of evidence and guidance. See the into practice pages for more information.

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Guideline Centre. Asthma: diagnosis, monitoring and chronic asthma management. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov 29. 38 p. (NICE guideline; no. 80).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Nov 29

Guideline Developer(s)

National Guideline Centre - National Government Agency [Non-U.S.]

Source(s) of Funding

The National Guideline Centre was commissioned by the National Institute for Health and Care Excellence to undertake the work on this guideline.

Guideline Committee

Guideline Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all GC members declared interests including consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent Guideline Committee (GC) meetings, members declared arising conflicts of interest.

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B of each full guideline (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

This meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub or eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

Asthma: diagnosis and monitoring of asthma in adults, children and young people. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. 323 p. (NICE guideline; no. 80). Available from the National Institute for Health and Care Excellence (NICE) Web site .

Asthma: diagnosis and monitoring of asthma in adults, children and young people. Appendices. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. 888 p. (NICE guideline; no. 80). Available from the NICE Web site .

Chronic asthma management. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. 372 p. (NICE guideline; no. 80). Available from the NICE Web site .

Chronic asthma management. Appendices. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. 739 p. (NICE guideline; no. 80). Available from the NICE Web site .

Asthma: diagnosis, monitoring and chronic asthma management. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. (NICE guideline; no. 80). Available from the NICE Web site .

Asthma: diagnosis, monitoring and chronic asthma management. Resource impact report. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. 18 p. (NICE guideline; no. 80). Available from the NICE Web site .

Asthma diagnosis and monitoring. Resource impact template. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. (NICE guideline; no. 80). Available from the NICE Web site .

Chronic asthma management. Resource impact template. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. (NICE guideline; no. 80). Available from the NICE Web site .

Inhaled corticosteroid doses for NICE's asthma guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. 3 p. (NICE guideline; no. 80). Available from the NICE Web site .

Developing NICE guidelines: the manual. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Oct. Available from the NICE Web site .

Patient Resources

The following is available:

Asthma: diagnosis, monitoring and chronic asthma management. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2017 Nov. (NICE guideline; no. 80). Available from the National Institute of Health and Care Excellence (NICE) Web site . Also available in Welsh from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on April 23, 2018. The guideline developer agreed to not review the content.

This NEATS assessment was completed by ECRI Institute on January 8, 2018. The information was verified by the guideline developer on February 7, 2018.

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